REMARKS

In accordance with the Examiner's comment on page 2 of the Communication of August 18, 2003, the specification has been amended on pages 3-6, to italicize the names of bacteria genera and species of microorganisms. Similarly, where appropriate, the genera and species names of bacteria in the claims have been italicized where that was not previously done.

It is suggested in the Communication of August 18, 2003 (page 2) that the recitation of "about 250 g/L" glutamine, and "about 250 mM" glutamine in claims 10 and 35 respectively are inconsistent. It is submitted that such recitations are not inconsistent and are fully supported by the disclosure on page 9 of the application. In the case of "250 mM" glutamine, the glutamine reactant is in solution in the incubation solution. In the case of "250 g/L glutamine, the glutamine reactant is present in the incubation solution initially as a solid, i.e., as a slurry. Thus, it is appropriate to refer to a material in solution by the expression "mM" (millimole), while it is also appropriate to refer to a solid material in a slurry by the expression "g/L" (grams/liter). Reconsideration is respectfully requested.

It is also suggested in the Communication of August 18, 2003 that claims 10 and 35 be amended to recite a range of "about 25 mM to about 250 mM...glutamine." Such an amendment would unreasonably narrow such claims and would be inconsistent with the disclosure on page 9 of the application, which states that the glutamine reactant is present in amounts of "at least about" 250 mM and "at least about" 250 g/L. See lines 4 and 9-10 on page 9. Reconsideration is respectfully requested.

The withdrawal of the rejection under 35 U.S.C. 112, second paragraph, with respect to the need for a deposit of bacteria is acknowledged.

Rejection under 35 U.S.C. 112

Claims 5-8 and 14-15 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as his invention. Reconsideration is respectfully requested in view of the amendments to these claims. In particular, claim 5 has been amended by deleting the phrase "over a time period." Claim 6 has been amended by adding the phrase "when the desired amount of product comprising 2-oxoglutaramate is produced." Claims 7 and 8 have been amended by defining the oxoglutaramate product as the "product comprising 2-oxoglutaramate." Finally, as suggested by the Examiner, claim 14 has been amended in step (a) to read "said incubation solution slurry." Such amendments obviate the indefiniteness rejection under 35 U.S.C. 112, second paragraph. Reconsideration and withdrawal of the rejection under 35 U.S.C. 112 is respectfully requested.

Rejection under 35 U.S.C. 103 (a)

Claims 1-3, 5-11, 13-15, 31 and 33-40 remain rejected under 35 U.S.C. 103 (a) as being unpatentable over the article by Meister taken with the article by Szwajcer et al for the reasons of record with particular respect to unknown strains of *Providencia* or *Proteus* or active enzymes thereof. This rejection is respectfully traversed with respect to all of Applicant's pending claims.

The Examiner has acknowledged that Applicant's claims, which are directed to the specific enzymes of *Providencia* or *Proteus* cells described in the application, are not obvious and hence patentable. See the second paragraph on page 4 of the communication of August 18, 2003. Notwithstanding, it appears that the Examiner maintains that the rejected claims remain unpatentable because they include

unknown strains of *Providencia* or *Proteus* or "active" enzymes thereof. Such a rejection is unfounded based on the instant record.

Section 706.02(j) of the Manual of Patent Examining Procedure states the following

:

> "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. [case citations]"

> The initial burden is on the examiner to provide some suggestion of the
>
> desirability of doing what the inventor has done. To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references.

The underlying premise of the stated basic criteria for an obviousness-type rejection is that there must be a reference or references that expressly or impliedly

provide the required suggestion, motivation and expectation of success. In the case at hand, not only has no reference been cited which suggests the "unknown strains of *Providencia* or *Proteus* or active enzymes thereof" referred to in the rejection; but, moreover, no reference has been cited that describes or suggests the use of any such unknown strain of *Providencia* or *Proteus* or active enzymes thereof in Applicant's claimed invention. The rejection under 35 U.S.C. 103(a) is therefore not well founded because no *prima facie* case of obviousness has been established, as required by the MPEP and the case law. Reconsideration and withdrawal of this rejection is respectfully requested.

As noted in Applicant's response under 37 CFR 1.111, the primary reference, Meister, discloses the enzymatic oxidative deamination of Glutamine using snake venom in the presence of catalase. It is acknowledged in the original rejection that Meister does not disclose oxidative deamination of L-glutamine using bacterial cells or biocatalysts, much less such bacterial materials obtained from *Providencia* or *Proteus*, more particularly *Providencia* PCM 1270 and PCM 1298, or *Proteus mirabilis* PCM 1353. Accordingly, the Meister article does not disclose or suggest "unknown strains" of *Providencia* or *Proteus* or "active enzymes thereof." To supply the deficiency of the primary Meister reference, the rejection relies upon the article by Szwajcer et al.

Szwajcer et al discloses the testing of certain bacteria, including those belonging to the genera *Proteus* and *Providencia*, (including *Proteus mirabilis* and *Providencia sp* PCM 1270 and PCM 1298) for their capacity to oxidize certain amino acids to their corresponding alpha-keto acids. Notably, L-glutamine was not tested by Szwajcer et al.

Applicant's detailed discussion of the references, the rejection under 35 U.S.C. 103(a) and why the combination of these references do not make obvious Applicant's claimed invention is found in Applicant's response under 37 CFR 1.111

filed on June 19, 2003. For purposes of brevity, that entire discussion is incorporated herein and will not be repeated here.

In summary, however, the foregoing response established that one skilled in the art would not conclude from the Meister and Szwajcer et al references that L-glutamine would be converted to its corresponding alpha keto acid using *Providencia sp* 1298 for the reasons that (1) L-glutamine was not tested by Szwajcer et al, (2) L-glutamine is not structurally similar to L-tyrosine, and (3) the disclosure of Szwajcer et al does not provide one skilled in the art sufficient information from which a predictable pattern of L-amino acid oxidase activity to *Providencia sp* 1298 can be derived.

Considering the present record, it is respectfully submitted that the Examiner has not established a *prima facie* case of obviousness. Reconsideration of the rejection under 35 U.S.C. 103 is respectfully requested.

In the event that the Examiner considers any matter raised in the communication of August 18, 2003 to be still unresolved, the Examiner is invited to phone Applicant's representative at the number indicated below in order to expedite the resolution of any such matter. Should the Examiner maintain any of the rejections made in that communication, entry of the amendments proposed in this response is respectfully requested subject to the filing by Applicant of a Notice of Appeal to the Board of Patent Appeals and Interferences.

Respectfully submitted,

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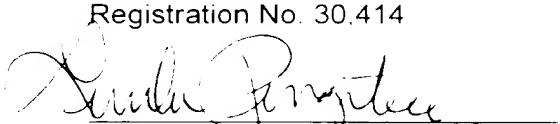

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September 10, 2003

Please amend the specification as follows:

Amend the paragraph bridging pages 3 and 4 to read as follows:

The method for producing 2-oxoglutaramate includes incubating ~~Providencia~~ *Providencia* or ~~Proteus~~ *Proteus* bacteria or an active biocatalyst obtained from such bacteria in an incubation solution comprising at least about 25mM (millimolar) of L-glutamine. Specific ~~Providencia~~ *Providencia* and ~~Proteus~~ *Proteus* strains include, without limitation, ~~Providencia sp~~*Providencia sp*. PCM-1298, ATCC Deposit No. PTA-3563, ~~Providencia sp~~*Providencia sp*. PCM-1270, ATCC Deposit No PTA-3564, and ~~Proteus mirabilis~~*Proteus mirabilis* PCM-1353, ATCC Deposit No. PTA-3562. The L-glutamine typically is added to the incubation solution prior to addition of the bacteria. Additionally, or alternatively, L-glutamine may be added to a culture already containing bacteria. The L-glutamine may be added as a single aliquot, or continuously over a period of time, for continuous-feed processes, either in two or more aliquots or as a steady trickle. The incubation solution may be an aqueous slurry comprising solid L-glutamine.

Amend page 5, lines 6-21 to read as follows:

Described herein is a method for producing 2-oxoglutaramate, a chemical compound with value as a plant growth regulator. Current manufacturing methods for producing 2-oxoglutaramate are not commercially practicable. The method of the present invention is a process by which L-glutamine is incubated in the presence of bacteria of the ~~Providencia~~ *Providencia* genus, such as ~~Providencia sp~~*Providencia sp*., and including ~~Providencia~~ *Providencia* strains PCM-1270, ATCC Deposit No. PTA-3564, and PCM-1298, ATCC Deposit No. PTA-3563, and/or bacteria of the ~~Proteus~~ *Proteus* genus, for instance ~~Proteus mirabilis~~*Proteus mirabilis*, such as strain PCM-1353, ATCC Deposit No. PTA-3562, each of which were deposited on July 25, 2001 at the

American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209, U.S.A. The designation "PCM-XXXX" refers to accession numbers of the Polish Collection of Microorganisms, Institute of Immunology and Experimental Therapy, Wroclaw, Poland.

Please amend page 6, lines 12-16 to read as follows:

(II) Szwajcer E. et al. ~~Providencia~~ *Providencia* medium

(Enzyme Microbiol. Tech., 1982, Vol. 4, pp 409-413)

10g/L bactopeptone

2g/L casein hydrolysate

2g/L yeast extract

6g/L NaCl or 10mm CaCl2

Please amend the claims to read as follows:

1. (currently amended) A method for producing 2-oxoglutaramate, comprising the step of incubating bacteria of the genera ~~Providencia~~ *Providencia* or ~~Proteus~~*Proteus*, or an active biocatalyst obtained from either of said bacteria, in an incubation solution comprising at least about 25 mM L-glutamine for a time sufficient to produce a product comprising 2-~~oxoglutamarate~~oxoglutaramate

2. (original) The method of claim 1, in which the incubation solution comprises at least about 100mM L-glutamine.

3. (original) The method of claim 1, in which the incubation solution comprises a buffer and catalase and has a pH ranging from 6.5 to 8.5.

4. (canceled)

5. (currently amended) The method of claim 1, in which L-glutamine is added to the incubation solution during incubation ~~over a time period~~ either in two or more aliquots or as a steady trickle.

6. (currently amended) The method of claim 1, further comprising the step of stopping the incubation when the desired amount of product comprising 2-oxoglutaramate is produced by either killing the bacteria, disrupting the bacteria or removing the bacteria from the incubation solution.

7. (currently amended) The method of claim 1, further comprising the step of purifying the product comprising 2-oxoglutaramate ~~product~~ by ion exchange chromatography.

8. (currently amended) The method of claim 1, further comprising the step of purifying the product comprising 2-oxoglutaramate ~~product~~ by precipitation.

9. (original) The method of claim 1, in which the incubation solution is a slurry comprising solid L-glutamine.

10. (original) The method of claim 9 in which the slurry comprises up to about 250 g/L of solid L-glutamine.

11. (currently amended) The method of claim 1 in which the bacteria is ~~Proteus mirabilis~~*Proteus mirabilis*.

12. (canceled)

13. (previously amended) The method of claim 1, in which the active biocatalyst is immobilized on a substrate.

14. (currently amended): A method for producing 2-oxoglutaramate, comprising the steps of:

a) providing an incubation solution slurry comprising a buffer and solid L-glutamine, said incubation solution slurry having a pH of from about 7.0 to about 8.0;

b) adding to the incubation solution slurry a resuspended wet cell pellet of a ~~Providencia~~*Providencia* culture or a ~~Proteus~~*Proteus* culture; and

c) incubating the slurry to convert L-glutamine to 2-oxoglutaramate.

15. (original) The method of claim 14, in which the slurry further comprises catalase.

16. (previously amended) A reaction mixture for producing 2-oxoglutaramate, comprising *Providencia* or *Proteus* bacteria or an active biocatalyst obtained from either of said bacteria, and at least about 25 mM L-glutamine, said bacteria or active biocatalyst having the capacity to convert L-glutamine to 2-oxoglutaramate.

17. (canceled)

18. (previously amended) The reaction mixture of claim 16, in which the bacteria is *Proteus mirabilis*.

19. (canceled)

20. (original) The reaction mixture of claim 16, comprising a near-saturation amount of L-glutamine.

21. (original) The reaction mixture of claim 16, comprising a slurry of solid L-glutamine.

22. (previously amended) The reaction mixture of claim 21, in which the slurry comprises up to about 250g/L of solid L-glutamine.

23. (original) The reaction mixture of claim 16, further comprising catalase.

24. (previously amended) The reaction mixture of claim 16, comprising an active biocatalyst obtained from *Providencia* or *Proteus* bacteria that is immobilized on a substrate.

25. (original) The reaction mixture of claim 16, comprising at least about 1% w/v, wet cell pellet mass, of the bacteria cells.

26. (original) The reaction mixture of claim 21, comprising from 1% by weight to 50% by weight bacteria (wet cell pellet mass), 50mM TRIS-HCl (pH 7.0 to 8.0), catalase and from 0.32% by weight to 25% by weight L-glutamine.

27. (original) A composition comprising *Providencia* or *Proteus* bacteria and at least about 20mM 2-oxoglutaramate.

28. (canceled)

29. (previously amended) The composition of claim 27, in which the bacteria is *Proteus mirabilis*.

30. (canceled)

31. (previously presented) A method for producing 2-oxoglutaramate, comprising the steps of (a) incubating bacteria of the genera *Providencia* or *Proteus*, or an active biocatalyst obtained from either of said bacteria, in an incubation solution comprising at least about 25mM of L-glutamine for a time

sufficient to produce a product comprising 2-oxoglutaramate, and (b) separating a material comprising 2-oxoglutaramate from said incubation solution.

32. (canceled)

33. (currently amended) The method of claim ~~32~~ 44 wherein the incubation solution has a pH of from about 6.5 to about 8.5.

34. (previously presented) The method of claim 33 wherein the period of incubation is from about 1 to about 24 hours.

35. (currently amended) The method of claim ~~32~~ 44 wherein the incubation solution comprises at least about 250mM of L-glutamine.

36. (previously presented) The method of claim 33 wherein the concentration of L-glutamine in the incubation solution is near saturation.

37. (currently amended) The method of claim ~~32~~ 44 further comprising purifying 2-oxoglutaramate separated from the incubation solution.

38. (previously presented) The method of claim 33 wherein the incubation solution comprises a buffer and has a pH of from about 7 to about 8.

39. (currently amended) The method of claim 31 wherein step (b) further comprises stopping the incubation by either killing the bacteria, disrupting the bacteria, or removing the bacteria from the incubation solution.

40. (previously presented) The method of claim 39 further comprising the step of purifying 2-oxoglutaramate product by ion exchange chromatography.

41. (not entered) A method for producing 2-oxoglutaramate, comprising the step of incubating the bacteria *Providencia sp.* PCM-1298, *Providencia sp.* PCM-1270, or *Proteus mirabilis* strain PCM-1353, or an active biocatalyst obtained from either of said bacteria, in an incubation solution comprising at least about 25mM L-glutamine for a time sufficient to produce a product comprising 2-oxoglutaramate.

42. (not entered) A reaction mixture for producing 2-oxoglutaramate, comprising the bacteria *Providencia sp.* PCM-1298, *Providencia sp.* PCM-1270, or *Proteus mirabilis* strain PCM-1353, or an active biocatalyst obtained from either of said bacteria, and at least about 25 mM L-glutamine, said bacteria or active biocatalyst having the capacity to convert L-glutamine to 2-oxoglutaramate.

43. (not entered) A composition comprising the bacteria *Providencia sp.* PCM-1298, *Providencia sp.* PCM-1270, or *Proteus mirabilis* strain PCM-1353 and at least about 20 mM 2-oxoglutaramate.

44. (not entered) A method for producing 2-oxoglutaramate, comprising the steps of (a) incubating bacteria *Providencia sp.* PCM-1298, *Providencia sp.* PCM-1270, or *Proteus mirabilis* strain PCM-1353, or an active biocatalyst obtained from either of said bacteria, in an incubation solution comprising at least about 25mM of L-glutamine for a time sufficient to produce a product comprising 2-oxoglutaramate, and (b) separating a material comprising 2-oxoglutaramate from said incubation solution.